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MEASUREMENT OF DIFFUSING CAPACITY FOR CARBON MONOXIDE (D_LCO)

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Single breath calculations of diffusing capacity for carbon monoxide (D_LCO) rely on the concentrations of carbon monoxide measured in the expired gas. Automated equipment generally collects data after the subject exhales a preset washout somewhat larger than the expected dead space. However, subjects with very high peak expiratory flows may exhale the washout volume before the gas analyzer step response has stabilized. A small sample volume recorded during rapid flow at that time may yield incorrectly low carbon monoxide concentrations, leading to falsely high D_LCO values. This report proposes that investigators inspect gas concentration vs. time graphs and choose the sample starting time to exclude the analyzer instability. This choice will result in a variety of washout volumes that are dependent on the peak expiratory flow generated by the subjects. Sample volumes of 1 L are recommended, to help to average out some of the experimental noise. The increased sample size adds less than 1 second to the 10-second breath-hold time.

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INTRODUCTION

Measurements of diffusing capacity for carbon monoxide (D_LCO) are often poorly reproducible. During recent work we became aware of a source of error related to gas analyzer response time correction. This report details the method we employed to eliminate that error. The approach applies to any situation in which the gas analyzer is either overcorrected or too slow.

The breath-holding (single breath) D_LCO measurement uses the difference between the amount of carbon monoxide inhaled and the amount present in the lungs at the end of the breath-hold to calculate the rate of its transfer. Amounts of gas can be determined from volumes and concentrations. The volume of gas inhaled is known by direct measurement, as is the inhaled concentration of carbon monoxide. The total lung volume during the breath-hold — that is, the sum of the volume inhaled and the residual gas in the lungs before the test gas is inhaled — can be calculated from dilution of a nonabsorbable tracer gas inhaled with the carbon monoxide. The concentration of carbon monoxide in the lungs is the only quantity difficult to obtain.

Exhaled gas concentration is a surrogate for the concentration in the lungs a short time earlier. The measurement is predicated on the assumption that the gas concentrations are uniform throughout the lungs. Then, once the dead space of the instrument and the airways have been flushed with gas from deep inside the lungs, the expired gas is assumed to represent the alveolar gas at the end of the contact time. However, gas transfer does not stop when expiration begins, though the contact area in the lungs shrinks progressively as lung volume decreases.

Our instruments (CPL and GS, Collins Medical; Braintree, MA) use a fast-response gas analyzers to measure a small gas sample immediately after the dead space washout, when lung volume is still high. After 0.5 L to 1 L of gas has been exhaled, the product of gas composition and flow is integrated until approximately 0.5 L of gas has passed the analyzer. The washout volume can be selected during the instrument setup phase. Either washout volume or sample volume can be changed on a by-measurement basis after the data have been acquired.

Any gas analyzer requires some time to respond to a change in gas composition, and a software correction may be applied to increase the effective response time of the instrument. However, some correction algorithms may cause the step response to overshoot. An example with overshoot is shown in fig. 1, and one without overshoot in fig. 2. Overshoot may occur not only during calibration, but also during measurements with a well-demarcated end to the dead space and very high expiratory flow (fig. 3). This is the usual pattern for the NEDU diver population. An unreliable estimate of D_LCO then is obtained in subjects whose expiratory flow is high, because the 0.5-L sample of expired gas begins during

the overshoot. It is less obvious that even without correction overshoot, in subjects whose expiratory flow is high, the 0.5-L sample of expired gas begins before the analyzer response has stabilized. If subjects have very high expiratory flows, the entire 0.5-L sample may be collected when the analyzer response is unreliable, whether or not step response overshoots occur.

Gas composition and volume expired were sampled and stored throughout the D_LCO maneuver. We investigated two post-processing methods to improve the reliability of D_LCO measurements: 1) delaying the start of sampling until after the analyzer response was stable, and 2) using a larger sample volume to average out the fluctuations.

METHODS

GENERAL

D_LCO measurements with analyzer overshoots evident were examined in detail for six subjects. Starting times (washout volumes) and sample volumes were adjusted, and the resulting diffusing capacities were calculated. Washout volumes used were either the preset 1 L or a volume selected to avoid the overshoot from the dynamic behavior of the analyzer. The starting time was advanced on the graphical concentration – time representation until it was past the correction overshoot. In some subjects, a larger or a smaller washout was tested as well. Sample volumes used were 0.5 L, 1 L, 2 L, and 3 L.

Several schemes for estimating gas-to-blood contact time can be selected during instrument setup. They all yield very similar times so long as the subject both inhales and exhales rapidly. We used the Jones-Meade method, in which contact time is considered to begin after the first third of inspiratory time and to end halfway into the sampling period. [1,2]

One set of data should produce one diffusing capacity, independent of sample size and washout values. The goal was to find the shortest washouts and smallest samples that yielded results consistent with the largest number of the other results. Thus, the individual diffusing capacities were compared to the average value from the same set of data.

RESULTS

At low sample volumes and low washout volumes the range in D_LCO with different washout volumes was as much as 7% of the average value for an individual subject (figs. 4 and 5). D_LCO converged to a range of about 2% around the average either when the sample volume was increased (fig. 4) or when the washout volume was increased (fig. 5). The values of diffusing

capacity were internally consistent for all sample volumes when the sampling began after the overshoot in the analyzer response (fig. 6). However, the coefficient of variation for the fraction of the overall average diffusing capacity for an individual was 2.6% for 0.5-L sample volumes and was less than 2% for the larger volumes. We standardized on a 1-L sample.

DISCUSSION

The washout time is the variable that needs to be chosen to accommodate the corrected analyzer response time. The initial expiratory flow determines what volume has passed before the gas composition readings are reliable. Thus, subjects with lower peak flows require smaller washout volumes than those with high peak expiratory flows. The dead space washout will be complete so long as the volume is at least 0.75 L. One can ensure that both requirements are met by starting the sample after gas concentration becomes a straight-line function of time.

Although larger sample volumes degrade the breath-hold contact-time estimates, they improve the reliability of the gas composition measurements. With the procedure we have adopted, the additional contact time at reduced lung volume is less than one second — that is, less than 10% of the contact time. Textbooks of respiratory physiology generally refer to larger or later gas samples than 0.5 L after washout of 1 L — namely, end-expiratory sampling,[3] mixed expired samples,[4] or one-liter samples.[5] If the gas sample impinges on expiratory reserve volume, the assumption that the composition is uniform throughout the lungs may be violated. However, in any subject, if the graph of the poorly soluble tracer gas concentration against time shows a constant concentration during sampling, the gas composition in the sample is uniform.

CONCLUSIONS/RECOMMENDATIONS

Clinical pulmonary function testing equipment should not be used with the default settings to measure D_LCO in healthy, well-trained subjects who can generate very rapid expiratory flows. We recommend adjusting the calculations to begin sampling after the gas concentration tracing appears stable, and to sample 1 L of expired gas to average out any remaining analyzer instability. A 1-L sample is contraindicated only if the tracer gas tracing is not flat between the sample markers, in which case the sample should be taken over a range with a constant concentration of tracer gas.

Many other sources of experimental error exist than that discussed above. For D_LCO measurements to be as reproducible as possible, the subject should:

1. sit comfortably straight,

2. exhale as fully as possible at a rapid rate,
3. inhale rapidly to nearly total lung capacity,
4. maintain the volume for 10 s with relaxed muscles by closing the glottis, blocking the mouthpiece, or using a valve in the equipment, and
5. exhale as rapidly as possible until the graph of volume exhaled as a function of time begins to plateau (fig. 3). The subject need not empty his or her lungs to residual volume.

By inhaling only to nearly full capacity, one avoids distending alveoli much more fully than normal. By relaxing with nearly full lungs instead of sustaining the inspiratory effort, one avoids drawing extra blood into the lung circulation during the measurement.

The operator should:

1. enter the correct hemoglobin concentration and carboxyhemoglobin percentage saturation. (On the Collins machines, under the "Modify" menu),
2. adjust the sample starting time (on the Collins machines, under the "Alter" menu) to a point where the graph of carbon monoxide concentration as a function of time has leveled off after the step change and dynamic response, and
3. adjust the sample end (on the Collins machines, under the "Alter" menu) for a sample volume as close as possible to 1 L.

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1. *Instruction Manual for the Collins Comprehensive Pulmonary Laboratory (CPL)*, (Braintree, MA: Collins Medical, Inc. January 2000).

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3. M. P. Hlastala, and A. J. Berger, *Physiology of Respiration*, 2nd ed. (New York, NY: Oxford University Press, 2001), p. 118.

4. A. E. Taylor, K. Rehder, R. E. Hyatt, and J. C. Parker, *Clinical Respiratory Physiology*. (Philadelphia, PA: W.B. Saunders Co., 1989), p. 46.

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Fig. 1 - Analyzer step response with overshoot in correction

RAPID RESPONSE DL ANALYZER CALIBRATION

PARAMETER	VALUE	RANGE	STATUS
CO OFFSET VOLTAGE	0.549	(-5.000 - 5.000)	Pass
CO GAIN	0.963	(0.700 - 1.300)	Pass
CO RESPONSE (msec)	135/ 75	(<220 / <110)	Pass
CO DELAY (msec)	300/260	(<600 / <500)	Pass
CH4 OFFSET VOLTAGE	0.717	(-5.000 - 5.000)	Pass
CH4 GAIN	0.985	(0.700 - 1.300)	Pass
CH4 RESPONSE (msec)	144/ 79	(<220 / <110)	Pass
CH4 DELAY (msec)	365/310	(<600 / <500)	Pass

Calibration Date: 12/17/2001

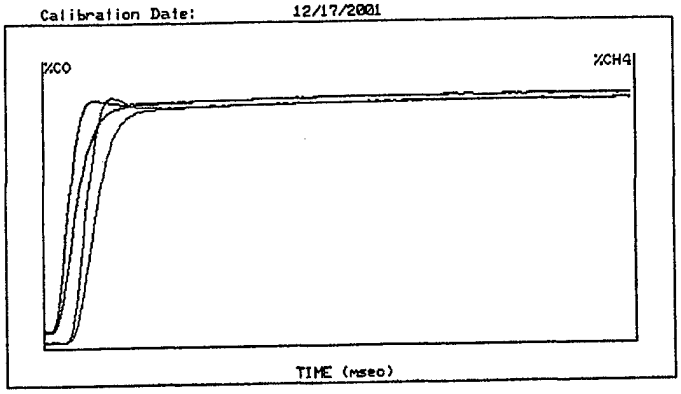

Fig.2 - Analyzer step response without overshoot

RAPID RESPONSE DL ANALYZER CALIBRATION

PARAMETER	VALUE	RANGE	STATUS
CO OFFSET VOLTAGE	-0.537	(-5.000 - 5.000)	Pass
CO GAIN	0.904	(0.700 - 1.300)	Pass
CO RESPONSE (msec)	144/ 76	(<220 / <110)	Pass
CO DELAY (msec)	372/328	(<600 / <500)	Pass
CH4 OFFSET VOLTAGE	-0.123	(-5.000 - 5.000)	Pass
CH4 GAIN	0.925	(0.700 - 1.300)	Pass
CH4 RESPONSE (msec)	162/ 76	(<220 / <110)	Pass
CH4 DELAY (msec)	429/376	(<600 / <500)	Pass

Calibration Date: 11/20/2001

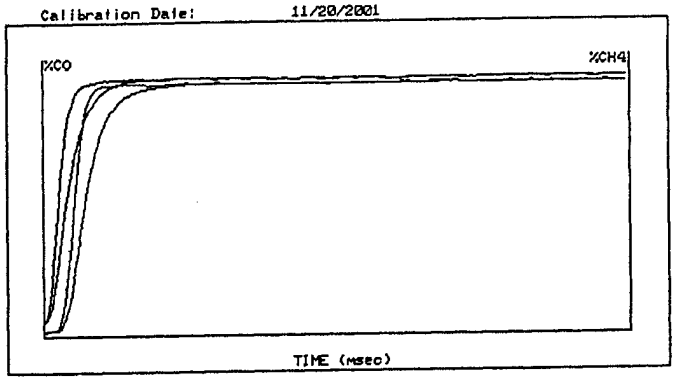

Fig. 3 - Experimental data showing analyzer overshoot

The sample starting time, marked by the first vertical bar, has been shifted past the overshoot, resulting in a washout volume of 1.8 L (Bottom row in the table). The sample end time has been moved to select a sample volume of 1.05 L, as displayed on the lower panel of the figure.

The small triangles on the time axes mark the default sample start and stop times, which put the sample entirely into the analyzer settling time.

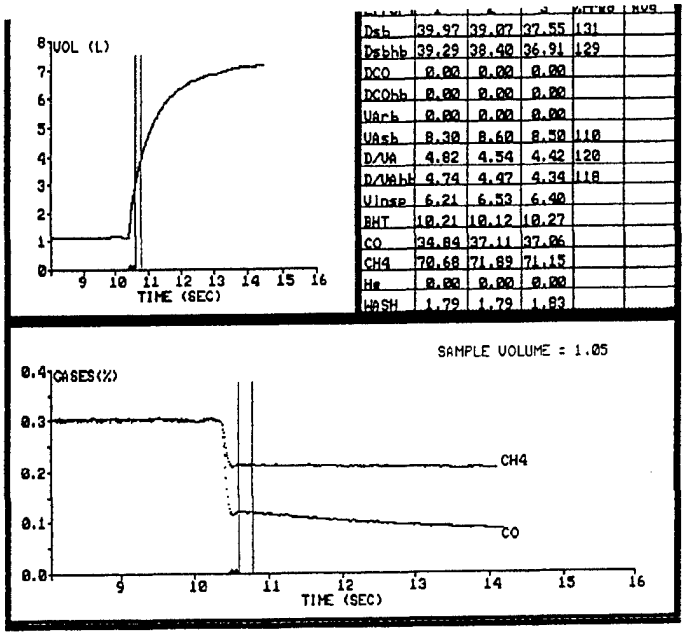

Fig. 4 - Effect of sample volume on D_LCO, different washouts

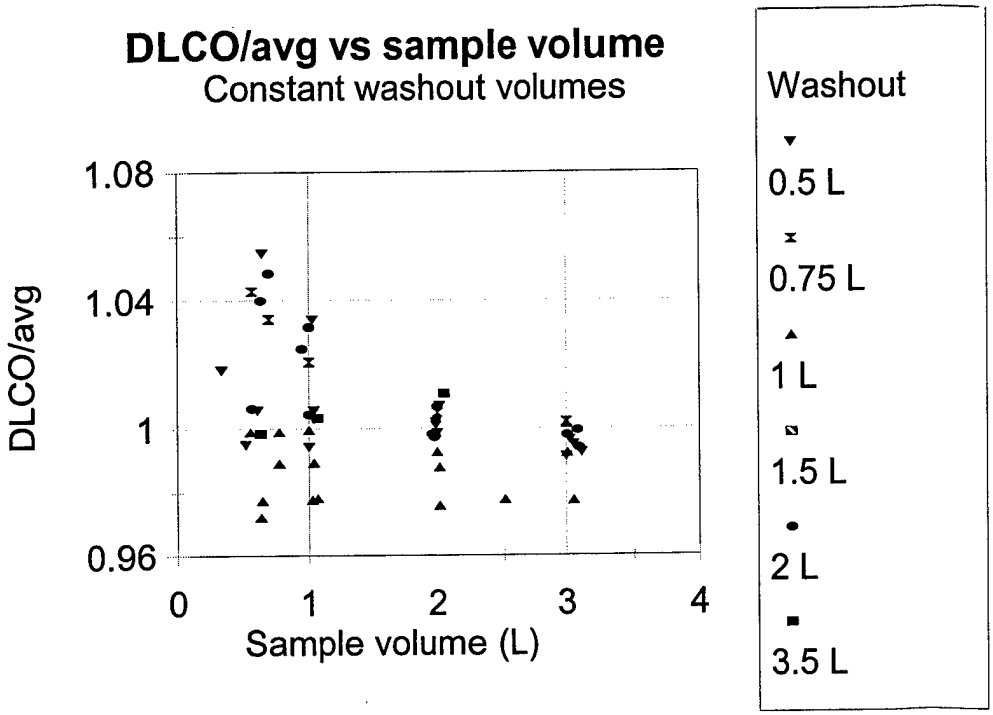

Fig. 5 - Effect of washout on D_LCO, different sample volumes

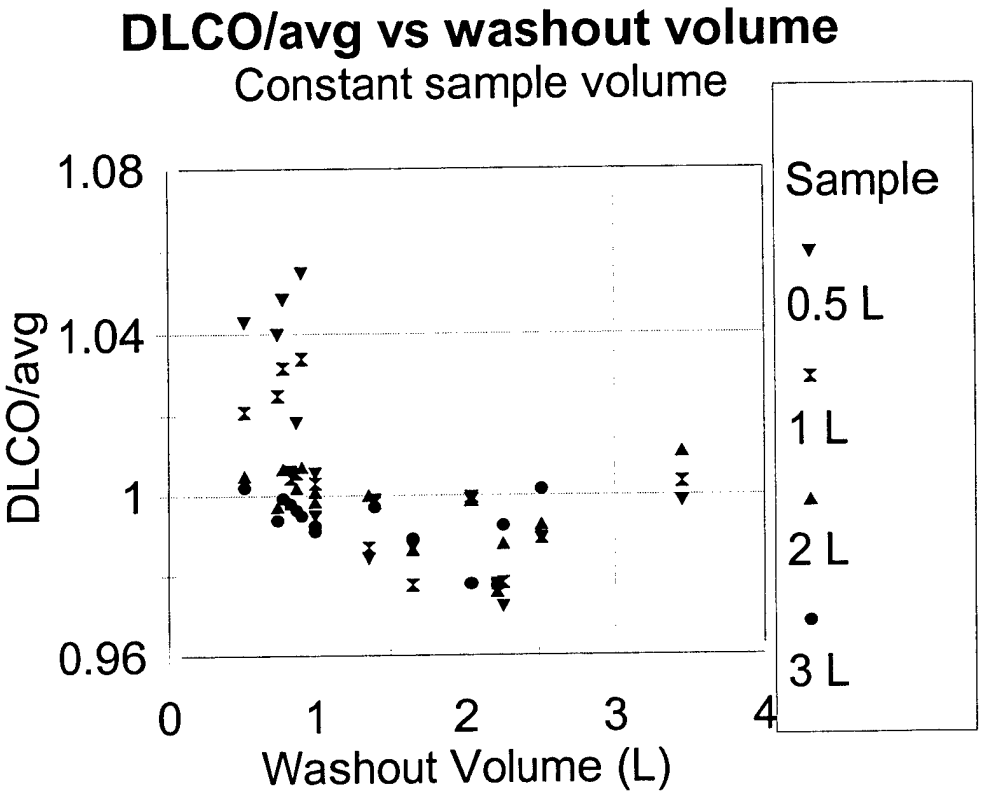

Fig. 6 - Effect of sample volume on D_LCO when analyzer stable